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10/550,866	09/23/2005	Dimitrios T Drivas	MP-02	1389

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EXAMINER	
MERTZ, PREMA MARIA	
ART UNIT	**PAPER NUMBER**
1646	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/550,866	DRIVAS ET AL.	
	Examiner	Art Unit	
	Prema M. Mertz	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 August 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) *3-6, 10-15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 7-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/30/07, 12/22/05, 9/23/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I (claims 1-2, and 7-9) and asthma as the species of disease to be treated, in the reply filed 8/22/07 is acknowledged. The traversal is on the ground(s) that the restriction is improper because the search and examination of the entire application would not entail a serious burden. However, contrary to Applicants arguments, the method claims are patentably distinct from the product claims because the method can be practiced with another product such as glucocorticoids. Furthermore, with respect to the peptide products recited in the peptide claims, any change of amino acid residues at any one or more positions in a polypeptide sequence is considered, absent factual data to the contrary, a patentably distinct polypeptide.

The PCT rules define a special technical feature as a feature, which defines a contribution over the prior art. The first claimed invention fails to recite such a feature, since Cytos Biotechnology (WO 03/040164, priority date 7/11/2001) teaches production and use of vaccines for the treatment of allergic diseases by administering a vaccine comprising a virus-like particle and at least one protein or peptide from IL-5, IL-13 and/or eotaxin bound thereto (see abstract). The method of the reference meets the limitations of the instant broad claims. Since the first claimed invention lacks a special technical feature, the other claimed inventions cannot share a special technical feature with the first claimed invention.

Furthermore, Applicants argue that the Examiners restriction is improper under 37 C.F.R. § 1.141(b) and M.P.E.P. § 806.05(i), which clearly state that where a national application contains claims to a product and a process for using that product, restriction is improper.

However, contrary to Applicants arguments, this application claims 123 patentably distinct amino acid sequences (SEQ ID NOs). Furthermore, Applicants have elected a method of using the product and not the product itself. The method can be practiced with a product, other than the instantly claimed products (SEQ ID NOs: 1-123). Therefore, the process of using the product and the products themselves, will not be examined together in the instant application.

The Groups as delineated in the restriction requirement 7/19/2007 are patentably distinct one from the other such that each invention could, by itself, in principle, support its own separate patent (as shown by the arguments put forth in the written restriction requirement).

The requirement is still deemed proper and is therefore made FINAL.

Claims 3-6, 10-15, are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Specification

2. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. It is suggested that the title be amended to recite the method claimed by administering the specific product and by deleting recitation of "preventing".

Claim Rejections - 35 USC § 112, first paragraph, scope of enablement

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3a. Claims 1-2, 7-9, are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating allergy comprising administering at least one of the peptides set forth in SEQ ID NOs: 1-38, 42-61, 117-121 and 130-132, and at least one of the peptides set forth in SEQ ID NOs: 62-116 and 122-123, does not reasonably provide enablement for a method for treating all types of inflammatory conditions by administering antibodies as recited in claim 1 or by administering two or more cytokines as recited in claim 7. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Claim 1, as written encompasses administering antibodies to eotaxin and IL-15 to a mammal to treat inflammation. The lack of working examples, lack of guidance in the specification and the prior art regarding administering antibodies to treat inflammation, greatly reduces the probability that one of skill in the art would successfully obtain the claimed invention without undue experimentation. Based on the information disclosed in the specification the ordinary artisan could not conclude that administration of antibodies will achieve a method of treatment of inflammation. Therefore, the instant invention is not enabled for the claimed scope of claim 1 by administering an anti-IL-5 antibody and an eotaxin antibody.

Furthermore, claims 2, 7-9, are drawn very broadly to methods of treating all types of disorders including inflammation ranging from inflammatory bowel disease to acute inflammatory demyelinating polyradiculoneuropathy (which is an autoimmune condition) by administration of eotaxin and IL-5. However, other than disclosing using at least one of the specific peptides set forth in SEQ ID NOs: 1-38, 42-61, 117-121 and 130-132, and at least one of the peptides set forth in SEQ ID NOs: 62-116 and 122-123 as a vaccine to treat asthma, the

specification fails to provide any guidance for the successful treatment of a disorder involving an immunomodulatory pathway, including HIV infection involving the TH-2 pathway, by administering the claimed antibody to a subject.

By application of the factors set forth in Ex parte Forman (230 USPQ 546 (Bd. Pat. App. & Int. 1986), and reiterated in In re Wands (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)), which include (1) quantity of experimentation, (2) guidance presented, (3) the predictability of the art, and (4) the breadth of the claims, in the instant application, the quantity of experimentation to determine which immunomodulatory pathways and which cytokines, from the various disparate cytokines, are encompassed by the scope of the claims is practically infinite and the guidance provided in the specification very little, thereby rendering the results of the methods taught in the specification unpredictable (see pages 26-28, Examples 10-11). Therefore, it would require undue experimentation to determine which cytokines would be encompassed by the scope of the method claims. The disclosure of peptides of IL-5 and eotaxin (pages 17-25) is clearly insufficient support under the first paragraph of 35 U.S.C. 112 for claims, which encompass a method of treating a disorder involving an immunomodulatory pathway by administering any two or more cytokines to elicit autoantibodies to the cytokines as recited in claim 7. In In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970), the Courts have held that: "Inventor should be allowed to dominate future patentable inventions of others where those inventions were based in some way on his teachings, since some improvements while unobvious from his teachings, are still within his contribution, since improvement was made possible by his work; however, he must not be permitted to achieve this dominance by claims which are insufficiently supported and hence, not in compliance with first paragraph of 35 U.S.C. 112; that

paragraph requires that the scope of the claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the art; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific law; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved."

There are substantial scientific reasons to doubt the scope of enablement, as set forth above. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. The specification does not describe administering any other peptides other than the peptides set forth in SEQ ID NOs: 1-38, 42-61, 117-121 and 130-132, and the peptides set forth in SEQ ID NOs: 62-116 and 122-123 as a vaccine to treat asthma, and since it is deemed to constitute undue experimentation to practice the invention as claimed, the disclosure is not commensurate with the scope of the claims. It is suggested that by employing conventional claim language, the method claims be amended to include in the method claim the specific cytokine peptides supported by the instant specification.

In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) states, "The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." "The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about

the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling" (MPEP 2164.03). The MPEP further states that physiological activity can be considered inherently unpredictable. Given the inherent unpredictability of physiological activity, which would include biological processes, i.e., methods of treatment, a certain amount of enablement beyond mere assertion must be required.

The method of the instant claims comprises the administration of cytokines for treatment of a disorder involving an immunomodulatory pathway. A first consideration would be the breadth of the claims. The specification on page 27, lines 23-30, and page 28, lines 1-3, discloses:

"Methods of Treating Inflammatory Conditions

The immunogens of the invention may also be administered in treatment regimens with other pharmaceuticals or anti-inflammatory agents. For example in the case of asthma or atopic chronic allergic disorders the patient may be actively immunized with art anti-eotaxin vaccine of the invention so as to control and down-regulate eotaxin levels and the accumulation of eosinophils in the affected tissues while at the same time a rescue medication or anti-asthma or anti-allergy agent is administered in response to an acute attack brought on for example by an overwhelming allergic stimulus. Such additional agents useful in combination treatments may include corticosteroids, cromoglyate, anti-inflammatories, COX-2 inhibitors, leukotriene (receptor) antagonists, xanthines, antihistamines and bronchodilators."

Except for this disclosure on pages 27-28, the instant specification does not adequately teach how to effectively treat a disorder involving an immunomodulatory pathway to reach a therapeutic endpoint by any combination of cytokines as recited in claim 7.

The CAFC decision (Genentech Inc. v. Novo Nordisk, 42 USPQ2d 1001, 1997) expressly states that:

"When there is no disclosure of any specific starting material or of any of the conditions under which a process can be carried out, undue experimentation is required; there is a failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art. It is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement".

For example, the treatment of inflammation has been the subject of intense study for the past several decades. Many promising treatments and therapies have been identified via in vitro experiments, and have not lived up to expectations when tested in vivo. In fact, the number of such treatments, which have failed to live up to their promise exceeds those, which have been performed as hoped by orders of magnitude. The disclosure fails to teach one of ordinary skill in the art a method of treating inflammation by administering a combination of any and all cytokines. With respect to the disparate tissues, the skilled artisan would have to undergo undue experimentation to determine if there is an effective amount of cytokines to be utilized for treating various conditions. It would not be reasonable to expect the cytokines to work on the various types of conditions because it is well known that results obtained on a tissue such as lung tissue are generally not reasonably predictive of results to be expected for neural and other

tissues. Furthermore, the disparate cytokines have disparate properties. Thus, it would require undue experimentation on the part of the skilled artisan to use the claimed method for treatment as recited, in the absence of sufficient information to predict the results with an adequate degree of certainty. In view of this unpredictability in the treatment of inflammation, there cannot be said to be any reasonable expectation of success at the in vivo application of a potential therapy, especially in view of the fact that the current specification as filed presents no working examples pertaining to the method of treatment of various conditions in vivo using cytokines. Therefore, a method as recited in claim 7 has not been enabled by the specification. Given the breadth of the claims in light of the predictability of the art as determined by the number of working examples, the level of skill of the artisan, and the guidance provided in the instant specification and the prior art of record, it would require undue experimentation for one of skill in the art to practice the claimed invention.

Claim Rejections - 35 USC § 112, first paragraph, written description

3b. Claims 7-9, are rejected under 35 U.S.C. 1 12, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

These claims are drawn to a method of treating a disorder by administering "any two or more cytokines". The claims do not require that the cytokines possess any particular conserved structure, or other disclosed distinguishing feature. Thus, the claims are drawn to a genus of cytokines that is defined only by involvement in an immunomodulatory pathway. To provide evidence of possession of a claimed genus, the specification must provide sufficient

distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a partial structure in the form of a recitation of percent identity. There is not even identification of any particular portion of the structure that must be conserved for the biological activity of the cytokines to be used in the claimed method. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics and structure/function relationship, the specification does not provide adequate written description of the claimed genus of cytokines to be used in the claimed method.

Vas-cath Inc. v. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the ad that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the written description' inquiry, whatever is *now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that (he or she) invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of cytokines to be used in the claimed method, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF'S were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence. Therefore, only a method of treating asthma by using at least one of the peptides set forth in SEQ ID NOs: 1-38, 42-61, 117-121 and 130-132, and at least one of the peptides set forth in SEQ ID NOs: 62-116 and 122-123 but not the full breadth of the claims meets the written description provision of 35 U.S.C. 112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 U.S.C. § 112, second paragraph

4. Claims 1-2, 7-9, are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1, line 3, is vague and indefinite because it recites "comprising autoantibodies to eotaxin and IL-5", which is unclear because it is uncertain whether the antibodies are generated or being administered.

Claim 2, is vague and indefinite because it is unclear whether the eotaxin and IL-5 are being administered.

Similarly, claim 1 is vague and indefinite because it is unclear whether the eotaxin and IL-5 are being administered.

Claim 7 is rejected as vague and indefinite because it recites "two or more cytokines". There is no upper limit on the number of cytokines being administered. Furthermore, the metes

and bounds of the claim are unclear because the claim fails to recite the specific cytokines to be administered.

Claims 8-9, are rejected are vague and indefinite insofar as they depend on claim 7 for its limitation.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in Graham v. John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5a. Claims 1-2, 7-9, are rejected under 35 U.S.C. 103(a) as unpatentable over WO 03/040164 ('164, priority date 11/7/2002).

The reference teaches a composition comprising a virus-like particle and at least one protein or peptide of IL-5, IL-13 and/or eotaxin bound thereto (see abstract; page 9 [0020]). The reference also teaches that the compositions are useful in the production of vaccines for the

treatment of allergic diseases and to induce self-specific immune responses by administering virus-like particles with a peptide of IL-5, IL-13 or eotaxin (see abstract; pages 112-113; page 125). The reference does not explicitly teach administering virus-like particles with both peptides of IL-5 and eotaxin to induce autoantibodies for the treatment of allergic diseases (inflammatory conditions).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, to modify the composition comprising the virus-like particle with IL-5 by addition of a second virus-like particle with eotaxin since '164 teaches the production and administration of virus-particles with these cytokine peptides to induce the production of antibody responses to these cytokines involved in inflammation. One of ordinary skill in the art would have been motivated to do so because the '164 patent teaches the production of vaccines with each of these components. Thus the artisan would have expected equal success using both components together to obtain a synergistic effect. To combine two compositions each of which is taught by the prior art to be useful for same purpose in order to form third composition that is to be used for very same purpose would have been obvious to one of ordinary skill in the art at the time the invention was made. The combination would have been obvious to the skilled artisan and the results achieved would have been expected (In re Kerkhoven, 205 USPQ 1069).

5b. Claims 1-2, 7-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 00/65058 ('058) in view of the Ponath et al. patent (U.S. Patent No. 7,265,201).

'058 discloses treating conditions such as asthma by downregulating IL-5 by enabling the production of antibodies against IL-5 by administering to a subject variants of IL-5 to induce production of cross-reactive antibodies capable of binding to autologous IL-5 (see abstract). However, the reference does not teach administering eotaxin to induce the production of anti-eotaxin antibodies to treat asthma.

Ponath et al. teaches administering peptides of eotaxin to be administered for immunization in the treatment of allergic conditions such as asthma(see abstract; column 13, lines 6-14; column 14, lines 13-24). However, the reference does not teach administering IL-5 to induce the production of anti-IL-5 antibodies to treat asthma.

Therefore, it would have been *prima* facie obvious to one having ordinary skill in the art at the time the invention was made, to modify the composition comprising the IL-5 peptides disclosed by '058 by addition of a second composition comprising eotaxin peptides as taught by Ponath et al since '164 teaches the production and administration of virus-particles with these cytokine peptides to induce the production of antibody responses to both these cytokines which are involved in inflammation. One of ordinary skill in the art would have been motivated to do so because both references teach the production of vaccines with each of these components. Thus the artisan would have expected equal success using both components together to obtain a synergistic effect. To combine two compositions each of which is taught by the prior art to be useful for same purpose in order to form third composition that is to be used for very same purpose would have been obvious to one of ordinary skill in the art at the time the invention was made. The combination would have been obvious to the skilled artisan and the results achieved would have been expected (In re Kerkhoven, 205 USPQ 1069).

Conclusion

No claim is allowed.

Claims 1-2, 7-9 are rejected.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Prema Mertz whose telephone number is (571) 272-0876. The examiner can normally be reached on Monday-Friday from 7:00AM to 3:30PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, can be reached on (571) 272-0835.

Official papers filed by fax should be directed to (571) 273-8300. Faxed draft or informal communications with the examiner should be directed to (571) 273-0876.

Information regarding the status of an application may be obtained from the Patent application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Prema Mertz Ph.D., J.D.
Primary Examiner
Art Unit 1646
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